

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Patricia A. Shatynski on 8-1-06.

The application has been amended as follows:

Claim 7 (amended): Page 2, delete the 4th, 5th and 6th compounds (or delete lines 25-32).

Page 3, delete the 3rd, 4th, 5th, 6th, 7th and 8th compounds (lines 5-17).

Cancel claims 13-24.

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Claim 1 (Presently Canceled)

Claim 2 (Presently Canceled)

Claim 3 (Presently Canceled)

Claim 4 (Presently Canceled)

Claim 5 (Presently Canceled)

Claim 6 (Presently Canceled)

Claim 7 (Presently Amended) **The A compound of ~~Claim 1~~ selected from the group consisting of:**

{[5-(2,4-Diaminopyrimidin-6-yl)pentanoyl]-(N-methyl)amino}-3-(6-methoxypyridin-3-yl)-propanoic acid;

{[5-(2,4-Diaminopyrimidin-6-yl)pentanoyl]-(N-methyl)amino-3(R)-(6-methoxypyridin-3-yl)-propanoic acid;

{[5-(2,4-Diaminopyrimidin-6-yl)pentanoyl]-(N-methyl)amino-3(S)-(6-methoxypyridin-3-yl)-propanoic acid;

~~{[5-(3-Amino-5,6,7,8-tetrahydroisoquinolin-1-yl)pentanoyl]-(N-methyl)amino}-3-(6-methoxypyridin-3-yl)-propanoic acid;~~

~~{[5-(3-Amino-5,6,7,8-tetrahydroisoquinolin-1-yl)pentanoyl]-(N-methyl)amino}-3(R)-(6-methoxypyridin-3-yl)-propanoic acid;~~

~~{[5-(3-Amino-5,6,7,8-tetrahydroisoquinolin-1-yl)pentanoyl]-(N-methyl)amino}-3(S)-(6-methoxypyridin-3-yl)-propanoic acid;~~

9-(2,4-Diaminopyrimidin-6-yl)-3-(quinolin-3-yl)-nonanoic acid;

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9-(2,4-Diaminopyrimidin-6-yl)-3(R)-(quinolin-3-yl)-nonanoic acid;

9-(2,4-Diaminopyrimidin-6-yl)-3(S)-(quinolin-3-yl)-nonanoic acid;

[~~3(2-Methyl-pyrimidin-5-yl)-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;~~

~~3(R)-(2-Methyl-pyrimidin-5-yl)-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;~~

~~3(S)-(2-Methyl-pyrimidin-5-yl)-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;~~

~~3-Pyrimidin-5-yl-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;~~

~~3(R)-Pyrimidin-5-yl-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;~~

~~3(S)-Pyrimidin-5-yl-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;~~]

(2-Methyl-pyrimidin-5-yl)-9-(1,4,5,6-tetrahydro-pyrimidin-2-ylcarbamoyl)-nonanoic acid;

3(R)-(2-Methyl-pyrimidin-5-yl)-9-(1,4,5,6-tetrahydro-pyrimidin-2-ylcarbamoyl)-nonanoic acid;

3(S)-(2-Methyl-pyrimidin-5-yl)-9-(1,4,5,6-tetrahydro-pyrimidin-2-ylcarbamoyl)-nonanoic acid;

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(dihydrobenzofuran-6-yl)-nonanoic acid;

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(dihydrobenzofuran-6-yl)-nonanoic acid;

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(dihydrobenzofuran-6-yl)-nonanoic acid;

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(6-methoxypyridin-3-yl)nonanoic acid;

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(6-methoxypyridin-3-yl)nonanoic acid;

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(6-methoxypyridin-3-yl)nonanoic acid;

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(2-methoxypyrimidin-5-yl)nonanoic acid;

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9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(2-methoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(2-methoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(quinoxalin-2-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(quinoxalin-2-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(quinoxalin-2-yl)nonanoic acid;
9-(2-Amino-4-ethylaminopyrimidin-6-yl)-3-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(2-Amino-4-ethylaminopyrimidin-6-yl)-3(R)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(2-Amino-4-ethylaminopyrimidin-6-yl)-3(S)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-aminopyrimidin-6-yl)-3-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-aminopyrimidin-6-yl)-3(R)-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-aminopyrimidin-6-yl)-3(S)-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(2-Ethylaminopyrimidin-6-yl)-3-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(2-Ethylaminopyrimidin-6-yl)-3(R)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(2-Ethylaminopyrimidin-6-yl)-3(S)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
and
3-(2-Methyl-pyrimidin-5-yl)-10-(1,4,5,6-tetrahydro-pyrimidin-2-ylamino)-decanoic acid;

or a pharmaceutically acceptable salt thereof.

Claim 8 (Previously Canceled)

Claim 9 (Presently Amended) A pharmaceutical composition comprising a compound according to Claim ~~4~~ 7 and a pharmaceutically acceptable carrier.

Claim 10 (Presently Withdrawn) The composition of Claim 9 which further comprises an active ingredient selected from the group consisting of

- a) an organic bisphosphonate or a pharmaceutically acceptable salt or ester thereof,
- b) an estrogen receptor modulator,
- c) an androgen receptor modulator,
- d) a cytotoxic/antiproliferative agent,
- e) a matrix metalloproteinase inhibitor,
- f) an inhibitor of epidermal-derived, fibroblast-derived, or platelet-derived growth factors,
- g) an inhibitor of VEGF,
- h) an antibody to a growth factor or a growth factor receptor,
- i) an inhibitor of Flk-1/KDR, Flt-1, Tck/Tie-2, or Tie-1,
- j) a cathepsin K inhibitor,
- k) a growth hormone secretagogue,
- l) an inhibitor of osteoclast proton ATPase,
- m) an inhibitor of urokinase plasminogen activator (u-PA),
- n) a tumor-specific antibody-interleukin-2 fusion protein,
- o) an inhibitor of HMG-CoA reductase, and
- p) a farnesyl transferase inhibitor or a geranylgeranyl transferase inhibitor or a dual farnesyl/geranylgeranyl transferase inhibitor;
and mixtures thereof.

Claim 11 (Presently Withdrawn) The composition of Claim 10 wherein said active ingredient is selected from the group consisting of

- a) an organic bisphosphonate or a pharmaceutically acceptable salt or ester thereof,
- b) an estrogen receptor modulator,
- c) an androgen receptor modulator,

- d) a cathepsin K inhibitor,
- e) an HMG-CoA reductase inhibitor, and
- f) an inhibitor of osteoclast proton ATPase;
and mixtures thereof.

Claim 12 (Presently Withdrawn) The composition of Claim 11 wherein said organic bisphosphonate or pharmaceutically acceptable salt or ester thereof is alendronate monosodium trihydrate.

~~**Claim 13 (Presently Withdrawn)** A method of eliciting an α_v integrin receptor antagonizing effect in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1.~~

Claim 14 (Presently Withdrawn) The method of Claim 13 wherein α_v the integrin receptor antagonizing effect is an $\alpha_v\beta_3$ antagonizing effect.

Claim 15 (Presently Withdrawn) The method of Claim 14 wherein the $\alpha_v\beta_3$ antagonizing effect is selected from the group consisting of inhibition of bone resorption, restenosis, angiogenesis, diabetic retinopathy, macular degeneration, inflammatory arthritis, cancer, and metastatic tumor growth.

Claim 16 (Presently Withdrawn) The method of Claim 15 wherein the $\alpha_v\beta_3$ antagonizing effect is the inhibition of bone resorption.

Claim 17 (Presently Withdrawn) A method of treating or preventing osteoporosis in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

Claim 18 (Presently Withdrawn) The method of Claim 12 wherein the α_v integrin receptor antagonizing effect is an $\alpha_v\beta_5$ antagonizing effect.

Claim 19 (Presently Withdrawn) The method of Claim 18 wherein the $\alpha_v\beta_5$ antagonizing effect is selected from the group consisting of inhibition of restenosis, angiogenesis, diabetic retinopathy, macular degeneration, inflammatory arthritis, cancer, and metastatic tumor growth.

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Claim 20 (Presently Withdrawn) ~~The method of Claim 13 wherein the αv integrin receptor antagonizing effect is a dual $\alpha v \beta 3 / \alpha v \beta 5$ antagonizing effect.~~

Claim 21 (Presently Withdrawn) The method of Claim 20 wherein the dual $\alpha v \beta 3 / \alpha v \beta 5$ antagonizing effect is selected from the group consisting of inhibition of bone resorption, restenosis, angiogenesis, diabetic retinopathy, macular degeneration, inflammatory arthritis, cancer, and metastatic tumor growth.

Claim 22 (Presently Withdrawn) A method of eliciting an αv integrin receptor antagonizing effect in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the composition of Claim 9.

Claim 23 (Presently Withdrawn) A method of treating or preventing a condition mediated by antagonism of an αv integrin receptor in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the composition of Claim 9.

Claim 24 (Presently Withdrawn) A method of treating metastatic tumor growth in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1 in combination with radiation therapy.

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